

Express Mail No.: EV 361 327 146 US

UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: CAPON *et al.*

Confirmation No.: 9120

Application No.: 09/875,082

Group Art Unit: 1636

Filed: June 5, 2001

Examiner: J. Ketter

For: COMPOSITIONS AND METHODS  
FOR DETERMINING ANTI-VIRAL  
DRUG SUSCEPTIBILITY AND  
RESISTANCE AND ANTI-VIRAL  
DRUG SCREENING

Attorney Docket No.: 11068-051-999  
(previously 50130-G)

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure provisions of 37 C.F.R. §1.56, there is hereby provided certain information which the Examiner may consider material to the examination of the subject U.S. patent application. It is requested that the Examiner make this information of record if it is deemed material to the examination of the application. This paper is being filed pursuant to C.F.R. § 1.34.

1. Enclosures accompanying this Information Disclosure Statement are:

1a. ☒ A list of all patents, publications, applications, or other information submitted for consideration by the office.

1b. A legible copy of :

☐ Each U.S. patent application publication and U.S. and foreign patent;

☒ Each publication or that portion which caused it to be listed on the PTO-1449;

☐ For each cited pending U.S. application, the application specification including the claims, and any drawing of the application, or portion of the application which caused it to be listed on the PTO-1449 including any claims directed to that portion;

☐ all other information or portion which caused it to be listed on the PTO-1449.

1c. ☒ An English language copy of search report(s) from a counterpart foreign application or PCT International Search Report.

1d. ☒ Explanations of relevancy (ATTACHMENT 1(d), hereto) or English language abstracts of the non-English language publications.

2. ☒ This Information Disclosure Statement is filed under 37 C.F.R. §1.97(b):

☐ Within three months of the filing date of a national application other than a continued prosecution application under §1.53(d);

- ☐ Within three months of the date of entry of the national stage as set forth in §1.491 in an international application;
- ☐ Before the mailing of the first Office action on the merits;
- ☒ Before the mailing of a first Office action after the filing of a request for continued examination under §1.114.

3. ☐ This Information Disclosure Statement is filed under 37 C.F.R. §1.97(c) after the period specified in 37 C.F.R. §1.97(b), but before the mailing date of any of a final action under 37 C.F.R. §1.113, a notice of allowance under 37 C.F.R. §1.311 or an action that otherwise closes prosecution in the application.

*(Check either Item 3a or 3b)*

- 3a. ☐ The Certification Statement in Item 5 below is applicable. Accordingly, no fee is required.
- 3b. ☐ The \$180.00 fee set forth in 37 C.F.R. §1.17(p) in accordance with 37 C.F.R. §1.97(c) is:
- ☐ enclosed
  - ☐ to be charged to Pennie & Edmonds LLP Deposit Account No. 16-1150.

*(Item 3b to be checked if any reference known for more than 3 months)*

4. ☐ This Information Disclosure Statement is filed under 37 C.F.R. §1.97(d) after the period specified in 37 C.F.R. §1.97(c), but on or before the date of payment of the issue fee.

The \$180.00 fee set forth in 37 C.F.R. §1.17(p) is:

- ☐ enclosed.
- ☐ to be charged to Pennie & Edmonds LLP Deposit Account No. 16-1150.

The Certification Statement in Item 5 below is applicable.

5. ☐ Certification Statement (applicable if Item 3a or Item 4 is checked)

*(Check either Item 5a or 5b)*

- 5a. ☐ In accordance with 37 C.F.R. §1.97(e)(1), it is certified that each item of information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement.
- 5b. ☐ Each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, and the communication was not **received** by any individual designated in 37 C.F.R. §1.56(c) more than thirty days prior to the filing of this information disclosure statement.
- 5c. ☐ Pursuant to 37 C.F.R. §1.704(d), each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart application, and the communication was not **received** by any individual designated in 37 C.F.R. §1.56(c) more than thirty days prior to the filing of this information disclosure statement.

6. ☒ This application is a continuation application under 37 C.F.R. §1.60 or §1.53(b) or (d).

(Check appropriate Items 6a, 6b and/or 6c)


- 6a. ☐ A Petition to Withdraw from issue under 37 C.F.R. §1.313(b)(5) is concurrently filed herewith.
- 6b. ☒ Copies of publications listed on Form PTO-1449 from prior application Serial Nos. 08/790,693 (now U.S. Patent 5,837,464) and 09/371,774 (now U.S. Patent 6,242,187), filed on January 29, 1997 and August 10, 1999, respectively, of which this application claims priority under 35 U.S.C. §120, are not being submitted pursuant to 37 C.F.R. §1.98(d). (Publications A01-A10 and A55-A159)
- 6c. ☒ Copies of the publications listed on Form PTO-1449 were not previously cited in prior application Serial Nos. 08/790,693 (now U.S. Patent 5,837,464) and 09/371,774 (now U.S. Patent 6,242,187), filed on January 29, 1997 and August 10, 1999, respectively, and are provided herewith. (Publications A11-A54)
7. ☐ This is a Supplemental Information Disclosure Statement. (Check Item 7a)
- 7a. ☐ This Supplemental Information Disclosure Statement under 37 C.F.R. §1.97(f) supplements the Information Disclosure Statement filed on . A bona fide attempt was made to comply with 37 C.F.R. §1.98, but inadvertent omissions were made. These omissions have been corrected herein. Accordingly, additional time is requested so that this Supplemental Information Disclosure Statement can be considered as if properly filed on .
8. ☐ In accordance with 37 C.F.R. §1.98, a concise explanation of what is presently understood to be the relevance of each non-English language publication is:

( Check Item 8a, 8b, or 8c)

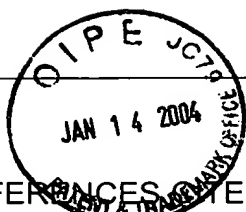
- 8a. ☐ satisfied because all non-English language publications were cited on the enclosed English language copy of the PCT International Search Report or the search report from a counterpart foreign application indicating the degree of relevance found by the foreign office.
- 8b. ☐ set forth in the application.
- 8c. ☐ enclosed as an attachment hereto.
9. ☒ The Commissioner is authorized to charge any additional fee required or credit any overpayment for this Information Disclosure Statement and/or Petition to Pennie & Edmonds LLP Deposit Account No. 16-1150.
10. ☒ No admission is made that the information cited in this Statement is, or is considered to be, material to patentability nor a representation that a search has been made (other than a search report of a foreign counterpart application or PCT International Search Report if submitted herewith). 37 C.F.R. §§1.97(g) and (h).

Respectfully submitted,

Date: January 14, 2004

  
Nikolaos C. George  
JONES DAY  
222 East 41<sup>st</sup> Street  
New York, New York 10017-6702  
(212) 326-3939

39,201  
(Reg. No.)



# LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

ATTY DOCKET NO.  
11068-051-999

APPLICATION NO  
09/875,082

APPLICANT  
Capon et al.

FILING DATE  
June 5, 2001

GROUP  
1636

## U.S. PATENT DOCUMENTS

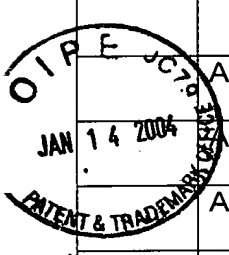
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLAS S	FILING DATE IF APPROPRIATE
	A01	4,952,496	8/1990	Studier et al.			
	A02	5,126,251	6/1992	Moss et al.			
	A03	5,135,855	8/1992	Moss et al.			
	A04	5,354,674	10/1994	Hodgson			
	A05	5,462,873	10/1995	Garfinkel et al.			

## FOREIGN PATENT DOCUMENTS

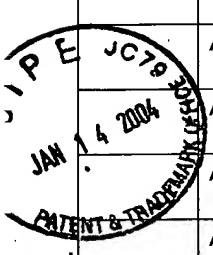
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	A06	WO91/19798	12/1991	PCT				
	A07	WO92/07943	5/1992	PCT				
	A08	WO94/19478	9/1994	PCT				
	A09	WO94/29438	12/1994	PCT				
	A10	WO95/22622	8/1995	PCT				
	A11	International Search Report PCT/US97/01609	4/1997	PCT				
	A12	International Search Report PCT/US98/15967	10/1998	PCT				

## OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

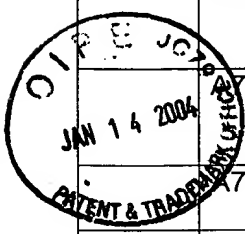
A13	Alam et al., "Reporter Genes: Application to the Study of Mammalian Gene Transcription," (1990), Analytical Biochemistry 188:245-254.
A14	Bernard, "Positive Selection of Recombinant DNA by CcdB," (1996), Biotechniques 21:320-323.
A15	Blight et al., "Efficient Initiation of HCV RNA Replication in Cell Culture," (2000), Science 290:1972-1974
A16	Chalfie, "Green Fluorescent Protein," (1995), Photochemistry and Photobiology, 62:651-656.
A17	Cheng et al., "Specific Interaction Between the Hepatitis C Virus Ns5B RNA Polymerase and the 3' End of the Viral RNA," (1999), J. Virol. 73:7044-7049.
A18	Chowrira et al., "In Vitro and in Vivo Comparison of Hammerhead Hairpin, and Hepatitis Delta Virus Self Processing Ribozyme Cassettes," (1994), J. Biol. Chem. 269: 25856-25864.
A19	Chung et al., "Hepatitis C Virus Replication is Directly Inhibited By IFN- $\alpha$ in a Full Length Binary Expression System," (2001), 98:9847-9852.
A20	Frese et al., "Interferon- $\gamma$ Inhibits Replication of Subgenomic and Genomic Hepatitis C Virus RNAs," (2002), Hepatology 35:694-703.
A21	Gould et al., "Firefly Luciferase as a Tool in Molecular and Cell Biology," (1988), Analytical Biochemistry 175:5-13.



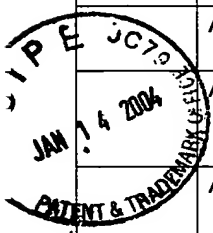
A22	Grakoui <i>et al.</i> , "Characterization of the Hepatitis C Virus-Encoded Serine Proteinase: Determination of Proteinase-Dependent Polyprotein Cleavage Sites," (1993), J. Virol. 67:2832-2843.
A23	Guo <i>et al.</i> , "Effect of Alpha Interferon on the Hepatitis C Virus Replicon," (2001) J. Virol. 75:8516-8523.
A24	Hiramatsu <i>et al.</i> , "HCV cDNA Transfection to HepG2 Cells," (1997), J. Viral Hepatol., 4(suppl.1):61-67.
A25	Hoshida <i>et al.</i> , "Improvement of Chemosensitivity Prediction by Transcriptional Profiling in Hepatoma Cells," (2001), Genome Informatics 12:257-58
A26	Ikeda <i>et al.</i> , "Selectable Subgenomic and Genome-Length Dicistronic RNAs Derived from an Infectious Molecular Clone of the HCV-N Strain of Hepatitis C Virus Replicate Efficiently in Cultured Huh7 Cells" (2002) J. Virol. 76:2997-3006.
A27	Kawai <i>et al.</i> , "α-Fetoprotein-Producing Hepatoma Cell Lines Share Common Expression Profiles of Genes in Various Categories Demonstrated by cDNA Microarray Analysis" (2001), Hepatology 33:676-691.
A28	Krieger <i>et al.</i> , "Enhancement of Hepatitis C Virus RNA Replication by Cell Culture-Adaptive Mutations," (2001), J Virol 75:4614-24.
A29	Lohmann <i>et al.</i> , "Replication of Subgenomic Hepatitis C Virus RNAs in a Hepatoma Cell Line" (1999), Science, 285:110-113.
A30	Lohmann <i>et al.</i> , "Mutations in Hepatitis C Virus RNAs Conferring Cell Culture Adaptation," (2001), J. Virol. 75:1437-1449.
A31	Mizutani <i>et al.</i> , "Characterization of Hepatitis C Virus Replication in Cloned Cells Obtained from a Human T-Cell Leukemia Virus Type 1-Infected Cell Line, MT-2," (1996), J. Virol. 70:7219-7223
A32	Moore <i>et al.</i> , "The Development of β-Lactamase as a Highly Versatile Genetic Reporter for Eukaryotic Cells," (1997) Analytical Chemistry 247:203-209.
A33	Mulligan <i>et al.</i> , "Expression of a Bacterial Gene In Mammalian Cells," (1980), Science 209: 1422-1427.
A34	Olesen <i>et al.</i> , "Detection of β-Glactosidase and β-Glucuronidase Using Chemiluminescent Reporter Gene Assays," Methods in Molecular Biology, Recombinant Protein Protocols: Detection and Isolation, 63:61-70.
A35	Perotta <i>et al.</i> , "A Pseudoknot-Like Structure Required for Efficient Self-Cleavage of Hepatitis Delta Virus RNA," (1991), Nature 350:434-436.
A36	Pflugheber <i>et al.</i> , "Regulation of PKR and IRF-1 During Hepatitis C Virus RNA Replication," (2002), PNAS 99: 4650-4655.
A37	Pietsch, <i>et al.</i> , "Characterization of the Continuous Cell Line HepT1 Derived from a Human Hepatoblastoma," (1996), Lab Invest 74:809-818.
A38	Pietschmann <i>et al.</i> , "Persistent and Transient Replication of Full Length Hepatitis C Virus Genomes in Cell Culture," (2002), J. Virol. 76:4008-4021.
A39	Schenborn <i>et al.</i> , "Reporter Gene Vectors and Assays," (1999), Molecular Biotechnology 13:29-44.
A40	Shimizu <i>et al.</i> , "Neutralizing Antibodies Against Hepatitis C Virus and the Emergence of Neutralization Escape Mutant Viruses," (1994), J. Virol. 68:1494-1500.
A41	Shimizu <i>et al.</i> , "Multicycle Infection of Hepatitis C Virus in Cell Culture and Inhibition by Alpha and Beta Interferons," (1994), J. Virol. 68:8406-8408.
A42	Shimizu <i>et al.</i> , "Correlation Between the Infectivity of Hepatitis C Virus <i>In Vivo</i> and its Infectivity <i>In Vitro</i> ," (1993), PNAS 90:6037-6041.
A43	Shimizu <i>et al.</i> , "Evidence for <i>In Vitro</i> Replication of Hepatitis C Virus Genome in a Human T-Cell Line," (1992), PNAS 89:5477-5481.
A44	Southern <i>et al.</i> , "Transformation of Mammalian Cells to Antibiotic Resistance with a Bacterial Gene Under Control of the SV40 Early Region Promoter," (1982), J. Molec. Appl. Genet. 1:327-341.
A45	Steinkühler <i>et al.</i> , "Activity of Purified Hepatitis C Virus Protease NS3 on Peptide Substrates," (1996), J. Virol. 70:6694-6700.
A46	Sugden <i>et al.</i> , "A Vector that Replicates as a Plasmid and can be Efficiently Selected in B-Lymphoblasts Transformed by Epstein-Barr Virus," (1985), Mol. Cell. Biol. 5, 410-413.



A47	Valli <i>et al.</i> , "Hepatitis C Virus Infection of a Vero Cell Clone Displaying Efficient Virus-Cell Binidng," (1997), Res. Virol. 148:181-186.
A48	Vassilev <i>et al.</i> , "Authentic and Chimeric Full-Length Genomic cDNA Clones of Bovine Viral Diarrhea Virus That Yield Infectious Transcripts," (1997), J. Virol. 71:471-478
A49	Wadkins <i>et al.</i> , "Ribozyme Activity in the Genomic and Antigenomic RNA Strands of Hepatitis Delta Virus," (2002), Cell Mol. Life Sci. 59:112-25.
A50	Witherell <i>et al.</i> , "Statistical Analysis of Combined Substitutions in Nonstructural 5A Region of Hepatitis C Virus and Interferon Responses," (2001), J. Med. Virol. 63:8-16.
A51	Wright-Minogue <i>et al.</i> , "Cross-Genotypic Interaction Between Hepatitis C Virus NS3 Protease Domains and NS4A Cofactors," (2000), J. Hepatology 32:497-504.
A52	Yang <i>et al.</i> , "Quantification of Gene Expression with a Secreted Alkaline Phosphatase Reporter System," (1997), BioTechniques 23:1110-1114.
A53	Yoo <i>et al.</i> , "Transfection of a Differentiated Human Hepatoma Cell Line (Huh7) with In Vitro-Transcribed Hepatitis C Virus (HCV) RNA and Establishment of a Long-Term Culture Persistently Infected With HCV," (1995), 69:32-38.
A54	Zlokarnik, "Fusions to $\beta$ -Lactamase as a Reporter for Gene Expression in Live Mammalian Cells," (2000), Methods in Enzymology 326:221-241.
A55	Danos, Olivier and Mulligan, Richard C. "Safe and Efficient Generation of Recombinant Retroviruses with Amphotropic and Ecotropic Host Ranges" Proc. Natl. Acad Sci. USA (Sep. 1988) vol. 85, pp. 6460-6464.
A56	Fuerst, Thomas R., and Moss, Bernard "Structure and Stability of mRNA Synthesized by Vaccinia Virus-encoded Bacteriophage 17 RNA Polymerase in Mammalian Cells" J. Mol. Biol. (1989) vol. 206, pp. 333-348.
A57	Lieber, Andre, et al., "High Level Gene Expression in Mammalian Cells by a Nuclear 17-Phage RNAPolymerase" Nucleic Acids Research (1989) vol. 17, No. 21, pp. 8485-8493.
A58	Larder, Brendan A., et al., "HIV with Reduced Sensitivity to Zidovudine (AZT) Isolated During Prolonged Therapy "Science (Mar. 31, 1989) vol. 243, pp.1731-1734.
A59	Andreasson, K.I., et al., "Production of Pro-Opiomelanocortin (POMC) by a Vaccinia Virus Transient Expression System and In Vitro Processing of the Expressed Prohormone by POMC-converting Enzyme" FE.B.S Letters (May 1989) vol. 248, No. 1.2 pp. 43-47.
A60	Elroy-Stein, Orna, et al., "Cap-Independent Translation of mRNA Conferred by Encephalomyocarditis Virus 5' Sequence Improves the Performance of the Vaccinia Virus/ Bacteriophage T7 Hybrid Expression System" Proc. Natl. Acad. Sci. USA (Aug. 1989) vol. 86, pp. 6126-6130.
A61	Larder, Brendan A., and Sharon D.Kemp, "Multiple Mutations in HIV-1 Reverse Transcriptase confer High-Level Resistance of Zidovudine (AZT)" Science (Dec. 1089) vol. 246, pp. 1155-1158.
A62	Elroy-Stein, Orna and Bernard Moss, "Cytoplasmic Expression System Based on Constructive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells" Proc. Natl. Acad. Sci. USA (Spe. 1990) vol. 87, pp. 6743-6747.
A63	Page, Kathleen A., et al., "Construction and Use of a Human Immunodeficiency Virus Vector for Analysis of Virus Infectivity" Journal of Virology (Nov. 1990) vol. 64, No. 11, pp. 5270-5276.
A64	Moss, B et al., "New Mammalian Expression Vectors" Nature (Nov. 1990) vol. 348, pp. 91-92.
A65	Deng, Hong, et al., "High-Efficiency Protein Synthesis from T7 RNA Polymerase Transcripts in 3T3 Fibroblasts" GENE (1991)pp. 193-201.
A66	Goldman, Mark E., et al., "L-696,229 Specifically Inhibits Human Immunodeficiency Virus Type 1 Reverse Transcriptase and Possesses Antiviral Activity In Vitro" Antimicrobial Agents and Chemotherapy (May 1992) vol. 36, No. 5, pp. 1019-1023.
A67	Saari, Walfred, S., et al. "2-Pyridinone Derivatives: A New Class of Nonnucleoside, HIV-1 Spedivid Reverse Transcriptase Inhibitors" Journal of Medicinal Chemistry (1991) vol. 34, No. 9, pp. 2922-2925.
A68	Landau, Nathaniel, R., et al., "Pseudotyping with Human T-Cell Leukemia Virus Type I Broadens the Human Immunodeficiency Virus Host Range" Journal of Medicinal Chemistry (1991) vol. 34, No. 9, pp 2922-2925.

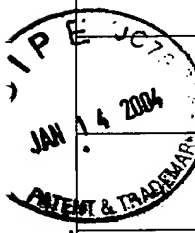


A69	Goldman, Mark E., et al., "Pyridinone Derivatives: Specific Human Immunodeficiency Virus Type 1 Reverse Transcriptase Inhibitors with Antiviral Activity" Proc. Natl. Acad. Sci. USA (Aug. 1991) vol. 88, pp. 6863-6867.
A70	Nunberg, Jack H., et al., "Viral Resistance to Human Immunodeficiency Virus Type-1 Specific Pyridinone Reverse Transcriptase Inhibitors" Journal of Virology (Sep. 1991) vol. 65, No. 9, pp. 4887-4892.
A71	St. Clair, M.H., et al. "Resistance to ddl and Sensitivity to AZT Induced by a Mutation in HIV-1 Reverse transcriptase" Science (Sep. 27, 1991) vol. 253, pp. 1557-1559.
A72	Huang, Mingjun and Summers, Jesse "Infection Initiated by the RNA Pregenome of a DNA Virus" Journal of Virology (Oct. 1991) vol. 65, No. 10, pp. 5435-543.
A73	Larder, Brendan, A., et al., "Zidovudine-Resistant Human Immunodeficiency Virus Selected by Passage in Cell Culture" Journal of Virology (Oct. 1991) vol. 65, No. 10, pp. 5232-5236.
A74	Homberger, F. R., et al. "Detection of Rodent Coronaviruses in Tissues and Cell Cultures by Using Polymerase Chain Reaction" J. Clin. Microbiol. (Dec. 1991) vol. 29:2789-2793.
A75	Sardana, Vinod, V, et al., "Functional Analysis of HIV-1 Reverse Transcriptase Amino Acids Involved in Resistance to Multiple Nonnucleoside Inhibitors" Journal of Biological Chemistry (1992) vol. 267, No. 25, pp. 17526-17530.
A76	Yang, Xian-Cbeng, et al., "Cell-Specific Posttranslational Events Affect Functional Expression at the Plasma Membrane but not Tetrodotoxin Sensitivity of the Rat Brain VIA Sodium Channel $\alpha$ -Subunit Expressed in Mammalian Cells" The Journal of Neuroscience (Jan. 1992) vol. 12(1), pp. 268-277.
A77	Richman, Douglas D. "Antiretroviral Drug Resistance: Mechanisms, Pathogenesis, Clinical Significance" pp. 1-13.
A78	Condra, Jon H., et al., "Identification of the Human Immunodeficiency Virus Reverse Transcriptase Residues That Contribute to the Activity of Diverse Nonnucleoside Inhibitors" Antimicrobial Agents and Chemotherapy (Jul. 1992) vol. 36, No. 7, pp. 1441-1446.
A79	Trono, Didier, "Partial Reverse Transcripts in Virions from Human Immunodeficiency and Murine Leukemia Viruses" Journal of Virology (Aug. 1992) vol. 66, No. 8, pp. 4893-4900.
A80	Lori, Franco, et al., "Viral DNA Carried by Human Immunodeficiency Virus Type 1 Virions" Journal of Virology (Aug. 1992) vol. 66, No. 8, pp. 5067-5074.
A81	Larder, Brendan A., "3' Azido-3'-Deoxythymidine Resistance Suppressed by a Mutation Conferring Human Immunodeficiency Virus Type 1 Resistance to Nonnucleoside Reverse Transcriptase Inhibitors" Antimicrobial Agents and Chemotherapy (Dec. 1992) vol. 36, No. 12, pp. 2664-2669.
A82	Gu, Zhengxian, et al., "Novel Mutation in the Human Immunodeficiency Virus Type 1 Reverse Transcriptase Gene That Encodes Cross-Resistance to 2',3'-Dideoxyinosine and 2',3'-Dideoxycytidine" Journal of Virology (Dec. 1992) vol. 66, No. 12, pp. 7128-7135.
A83	Baltimore, David, "The Treasure Under the Right Stone" Reverse Transcriptase (1993) pp. 1-3
A84	Larder, Brendan A., "Inhibitors of HIV Reverse Transcriptase as Antiviral Agents and Drug Resistance" Chapter 11 Reverse Transcriptase pp. 205-222 Cold Spring Harbor Laboratory Press (1993).
A85	Gao, Xiang, and Huang, Leaf, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes" Nucleic acids Research (1993) vol. 21, No. 12, pp. 267-2872.
A86	Gottesman, Michael M., and Pastan, Ira, "Biochemistry of Multidrug Resistance Mediated by the Multidrug Transporter" Annu. Rev. Biochem. (1993) vol. 62, pp. 385-427
A87	Le Grice, Stuart FJ., "Human Immunodeficiency Virus Reverse Transcriptase" Reverse Transcriptase (1993) pp. 163-191.
A88	Telesnitsky, Alice and Goff, Stephen P., "Strong-stop Strand transfer during Reverse Transcription" Reverse Transcriptase (1993) pp. 49-83.
A89	Wlodawer, Alexander and Erickson, John W., "StructureBased Inhibitors of HIV-1 1 Protease" Annu. Rev. Biochem. (1993) vol. 62, pp. 543-585.
A90	Richman, Douglas D., "HIV Drug Resistance" Annu. Rev. Pharmacol. Toxicol. (1993) vol. 32, pp. 149-164.
A91	Sandig, Volker, et al., "A Phage T7 Class-III Promoter Functions as a Polymerase II Promoter in Mammalian Cells" GENE (1993) pp. 255-259.

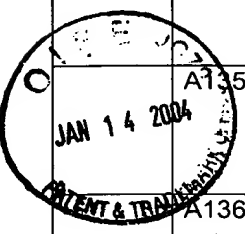


A92	Lieber, Andre, et al., "A Mutant T7 Phage Promoter is Specifically Transcribed by T7-RNA Polymerase in Mammalian Cells" <i>Eur. J. Biochem.</i> (1993) vol. 217, pp. 387-394.
A93	Chattopadhyay, Sisir K., et al., "Genomes of Murine Leukemia Viruses Isolated from Wild Mice" <i>Journal of Virology</i> (Sep. 1981) vol. 39, No. 3, pp. 777-791.
A94	Richman, Douglas D., "Minireview, Resistance of Clinical Isolates of Human Immunodeficiency Virus to Antiretroviral Agents" <i>Antimicrobial Agents and Chemotherapy</i> (June 1993) vol. 37, No. 6, pp. 1207-1213.
A95	Richardson, Jennifer H., et al., "Packaging of Human Immunodeficiency Virus Type 1 RNA Requires cis-Acting Sequences Outside the 5' Leader Region" <i>Journal of Virology</i> (July 1993) vol. 67, No. 7, pp. 3997-4005.
A96	Byrnes, Vera W., et al., "Comprehensive Mutant Enzyme and Viral Variant Assessment of Human Immunodeficiency Virus Type 1 Reverse Transcriptase Resistance to Nonnucleoside Inhibitors" <i>Antimicrobial Agents and Chemotherapy</i> (Aug. 1993) vol. 37, No. 8, pp. 1576-1579.
A97	Emimi, Emillo A., et al., "HIV-1 Error Revealed" <i>Nature</i> (Aug. 19, 1993) vol. 364, pp. 679.
A98	Balzarini, Jan et al., "Treatment of Human Immunodeficiency Virus Type 1 (HIV-1)-Infected Cells with Combinations of HIV-1-Specific Inhibitors Results in a Different Resistance Pattern Than Does Treatment with Single-Drug Therapy" <i>Journal of Virology</i> (Sep. 1993) vol. 67, No. 9, pp. 5353-5359.
A99	Larder, Brendan A., et al., "Convergent Combination Therapy can Select Viable Multidrug Multidrug-Resistant HIV-1 In Vitro" <i>Nature</i> (Sep. 30, 1993) vol. 365, pp. 451-453.
A100	Sag, Michael S., et al., "A short Term Clinical Evaluation of L-697,661, A Non-Nucleoside Inhibitor of HIV-1 Reverse Transcriptase" <i>The New England Journal of Medicine</i> (Oct. 7, 1993) vol. 329, No. 15, pp. 1065-1072.
A101	Boyer, Paul L. et al., "Mutational Analysis of the Fingers and Palm Subdomains of Human Immunodeficiency Virus Type-1 (HIV-1) Reverse Transcriptase" <i>J. Mol. Biology</i> (1994) vol. 243, pp. 472-483.
A102	Deng, Hong, and Wolff, Jon A., "Self-Amplifying Expression from the 17 Promoter in 3D Mouse Fibroblasts" <i>GENE</i> (1994) pp. 245-249.
A103	Richman, Douglas D., "Resistance, Drug Failure, and Disease Progression" <i>AIDS research and Human Retroviruses</i> (1994) vol. 10, No. 8, pp. 901-905.
A104	Ansari-Lari, M. Ali and Gibbs, Richard A., "Analysis of HIV Type 1 Reverse Transcriptase Expression in a Human Cell Line" <i>AIDS Research and Human Retroviruses</i> (1994) vol. 10, No. 9, pp. 1117-1124.
A105	Mirochnitchenki, Oleg, et al., "Production of Single-Stranded DNA in Mammalian Cells by Means of a Bacterial Retron" <i>The Journal of Biological Chemistry</i> (Jan. 1994) vol. 269, No. 4, pp. 2380-2383.
A106	Katz, Richard A., and Skalka, Anna Marie "The Retroviral Enzymes" <i>Annu. Rev. Biochem.</i> (1994) vol. 63, pp. 133-173.
A107	Chen, Xiaozhuo, et al., "A Self-Initiating Eukaryotic Transient Gene Expression System Based on Cotransfection of Bacteriophage T7 RNA Polymerase and DNA Vectors Containing a T7 Autogene" <i>NucleicAcids Research</i> (1994) vol. 22, No. 11, pp. 2114-2120.
A108	Kellam, Paul, et al., "Zidovudine Treatment Results in the Selection of Human Immunodeficiency Virus Type 1 Variants Whose Genotypes Confer Increasing Levels of Drug Resistance" <i>Journal of General Virology</i> (1994) vol. 75, pp. 341-351.
A109	Kellam, Paul, and Larder, Brendan A., "Recombinant Virus Assay: a Rapid, Phenotypic Assay for Assissment of Drug Susceptibility of Human Immunodeficiency Virus Type 1 Isolates" <i>Antimicrobial Agents and Chemotherapy</i> (1994) vol. 38, No. 1, pp. 23-30.
A110	El-Farrash, Mohamed A., et al., "Generation and Characterization of a Human Immunodeficiency Virus Type 1 (HIV-1) Mutant Resistant to an HIV-1 Protease Inhibitor" <i>Journal of Virology</i> (Jan. 1994) vol. 68, No. 1, pp. 233-239.
A111	Chen, Benjamin K., et al., "Distinct Modes of Human Immunodeficiency Virus Type 1 Proviral Latency Revealed by Superinfection of Nonproductively Infected Cell Lines with Recombinant Luciferase Encoded Viruses" <i>Journal of Virology</i> (Feb. 1994) vol. 68, No. 2, pp. 654-660.





A112	Richman, Douglas D., et al., "Nevirapine Resistance Mutations of Human Immunodeficiency Virus Type 1 Selected During Therapy" Journal of Virology (Mar. 1994) vol. 68, pp. 1660-1666.
A113	Ho, David D., et al., "Characterization of Human Immunodeficiency Virus Type 1 Variants with Increased Resistance to a C <sub>2</sub> -Symmetric Protease Inhibitor" Journal of Virology (Mar. 1994) vol. 68, No. 3, pp. 2016-2020.
A114	Boyer, Paul L. et al., "Sensitivity of Wild-Type Human Immunodeficiency Virus Type 1 Reverse Transcriptase to Dideoxynucleotides Depends on Template Length; The Sensitivity of Drug-Resistant Mutants Does Not" P.N.A.S. USE (May 1994) vol. 91, pp. 4882-4886.
A115	Brynes, Vera W., et al. "Susceptibilities of Human Immunodeficiency Virus Type 1 Enzyme and Viral Variants Expressing Multiple Resistance-Engendering Amino Acid Substitutions to Reverse Transcriptase Inhibitors" Antimicrobial Agents and Chemotherapy (Jun. 1994) vol. 38, No. 6, pp. 1404-1407.
A116	Parolin, Cristina, et al., "Analysis in Human Immunodeficiency Virus Type 1 Vectors of cis-Acting Sequences That Affect Gene Transfer into Human Lymphocytes" Journal of Virology (Jun. 1994) vol. 68, No. 6, pp. 3888-3895.
A117	Carroll, Richard, et al., "A Human Immunodeficiency Virus Type 1(HIV-1)-Based Retroviral Vectory System Utilizing Stable HIV-1 Packaging Cell Lines" Journal of Virology (Sep. 1994) vol. 68, No. 9, pp. 6047-6051.
A118	Richman, Douglas D., "Drug Resistance in Viruses" Trends in Microbiology (Oct. 10, 1994) vol. 2, No. 10, pp. 401-408.
A119	Zhang, Hui, et al., "Intravirion Reverse Transcripts in the Peripheral Blood Plasma of human Immunodeficiency Virus Type 1-Infected Individuals" Journal of Virology (Nov. 1994) vol. 68, No. 11, pp. 7591-7597.
A120	Kalderon, Daniel, et al., "A Short Amino Acid Sequence Able to Specify Nuclear Location" Cell (Dec. 1984 - Part 2) vol. 39, pp. 499-509.
A121	Ho, David D. "Time to Hit HIV, Early and Hard" The New England Journal of Medicine (1995) vol. 333, No. 7, pp. 450-451.
A122	Wyatt, Linda S., et al., "Replication-Deficient Vaccinia Virus Encoding Bacteriophage T7 RNA Polymerase for Transient Gene Expression in Mammalian Cells" Virology (1995) vol. 210, pp. 202-205.
A123	Ward, George A., et al., "Stringent Chemical and Thermal Regulation of Recombinant Gene Expression by Vaccinia Virus Vectors in Mammalian Cells" Proc. Natl. Acad. Sci. USA (1995) pp. 6773-6777.
A124	Wei, Xiping, et al., "Viral Dynamics in Human Immunodeficiency Virus Type 1 Infection" Nature Pan. 1995) vol. 373, pp. 117-122.
A125	Richman, Douglas D., "Drug Resistance in Relation to Pathogenesis" AIDS (1995) vol. 9 (Suppl A) pp. S49-S53.
A126	Volberding, Paul, "The Need for Additional Options in the Treatment of Human Immunodeficiency Virus Infection" The Journal of Infectious Diseases (1995) vol. 17 (Suppl 2) pp. S150-S154.
A127	Coffin, John M. "HIV Population Dynamics in Vivo: Implications for Genetic Variation, Pathogenesis, and Therapy" Science (Jan. 27, 1995) vol. 267, pp. 483-489.
A128	Kim Baek and Loeb Lawrence, A "Human Immunodeficiency Virus Reverse Transcriptase Substitutes for DNA Polymerase in Esherichia Coli" P.N.A.S. I vol. 92, pp. 684-688.
A129	Wain-Hobson, Simon "Virological Mayhem" Nature (Jan. 1995) vol. 373, p. 102.
A130	Ho, david D., et al., "Rapid Turnover of Plasma Virions and CD4 Lymphocytes in HIV-1 Infection" Nature (Jan. 1995) pp. 123-126.
A131	D'Aquila, Richard T., et al., "Zidovudine Resistance and HIV-1 Disease Progression During Antiretroviral Therapy" Annals of Internal Medicine (Mar. 15, 1995) vol. 122, No. 6, pp. 401-408.
A132	Condra, John H., et al., "In Vivo Emergence of HIV-1 Variants Resistant to Multiple Protease Inhibitors" Nature (Apr. 6, 1995) vol. 374, pp. 569-571.
A133	Boyer, Paul L., and Hughes, Stephen H., "Analysis of Mutations at Position 184 in Reverse Transcriptase of Human Immunodeficiency Virus Type 1" Antimicrobial Agents and Chemotherapy (Jul. 1995) vol. 39, No. 7, pp. 1624-1628.



A134	He, Jianglin, and Landau, Nathaniel R., "Use of a Novel Human Immunodeficiency Virus Type 1 Reporter Virus Expressing Human Placental Alkaline Phosphatase To Detect an Alternative Viral Receptor" <i>Journal of Virology</i> (Jul. 1995) vol. 69, No. 7, pp. 4587-4592.
A135	Kim, Baek and Loeb, Lawrence A., "A Screen in <i>Escherichia coli</i> for Nucleoside Analogs That Target Human Immunodeficiency Virus (HIV) Reverse Transcriptase: Coexpression of HIV Reverse Transcriptase and Herpes Simplex Virus Thymidine Kinase" <i>Journal of Virology</i> (Oct. 1995) vol. 69, No. 10, pp. 6563-6566.
A136	Saunders, J., and Cameron, J.M., "Recent Development in the Design of Antiviral Agents" <i>Med Res. Rev.</i> (Nov. 1995) vol. 15:497-531.
A137	Young, Steven D., et al., "L-743,726 (DMP-266): a Novel, Highly Potent Nonnucleoside Inhibitor of the Human Immunodeficiency Virus Type 1 Reverse Transcriptase" <i>Antimicrobial Agents and Chemotherapy</i> (Dec. 1995) vol. 39, No. 12, pp. 2602-2605.
A138	Goldman, Mark E., et al., "A Nonnucleoside Reverse Transcriptase Inhibitor Active on Human Immunodeficiency Virus Type 1 Isolates Resistant to Related Inhibitors!" <i>Antimicrobial Agents and Chemotherapy</i> (May 1993) vol 37, No. 5, pp. 947-949.
A139	Fang, Guowei, et al., "Molecular Cloning of Full-Length HIV-1 Genomes Directly from Plasma Viral RNA" <i>Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology</i> (1996) vol. 12, No. 4, pp. 352-357.
A140	Heid, Christian A., et al., "Real Time Quantitative PCR" <i>Genome Research</i> (1996) pp. 986-994.
A141	Romeyn, Mary, "Report from the 3rd Conference of Retroviruses and Opportunistic Infections" <i>BETA</i> (Mar. 1996).
A142	Schapiro, Jonathan, M., "Causes of Long Term Efficacy and/or Drug Failure in Protease (PR) Inhibitor Monotherapy" <i>ICA Abstracts</i> .
A143	Mamtora, gargi, et al., "HIV-1 Genechip™ and Dideoxynucleotide Sequence Analysis of HIV-1 Genomes Present in Plasma Samples from Patients of ACTG 143 Study" <i>ICA Abstracts</i> .
A144	Garrett, Miyada, C., et al., "Sequencing HIV Isolates Using the Genechip™ HIV PRT Assay" <i>ICA Abstracts</i> .
A145	Gingeras, Thomas R., et al. "Detection of Rifampin Conferring Mutations and Mycobacteria Speciation Using Myco Genechip™" <i>ICA Abstracts</i> .
A146	Fischl, Margaret A., "Treatment of HIV Infection" <i>Section II-Management of HIV Infections and Their Complications</i> , Chapter 8, pp. 141-160.
A147	Saag, Michael S. "AIDS Testing Now and in the Future" <i>Section I-The Virus: Its Transmission and Infection</i> , Chapter 4, pp. 65-88, 1994.
A148	Richman, Douglas, D., "Antiviral Drug Resistance: Issues and Challenges" <i>Antiviral Drug Resistance</i> , Introductory Chapter, pp. 1-19.
A149	Japour, Anthony J., "Standardized Peripheral Blood Mononuclear Cell Culture Assay for Determination of Drug Susceptibilities of Clinical Human Immunodeficiency Virus Type 1 isolates" <i>Antimicrobial Agents and Chemotherapy</i> (May 1993) vol. 37, pp. 1095-1101.
A150	Pauwels, Rudi, et al. "Rapid and Automated Tetrazoliumbased Colorimetric Assay for the Detection of anti-HIV Compounds" <i>Journal of Virological Methods</i> (1988) vol. 20, pp. 309-321.
A151	Larder, B. A., (1994) "Interactions Between Drug Resistance Mutations In Human Immunodeficiency Virus Type 1 Reverse Transcriptase" <i>Journal of General Virology</i> , 75:951-957.
A152	Piatak, Jr., M., et al. (1993) "High Levels of HIV-1 In Plasma During All Stages Of Infection Determined By Competitive PCR" <i>Science</i> 259:1749-1754.
A153	Popovic, M., et al. (1984) "Detection, Isolation, and Continuous Production Of Cytopathic Retroviruses (HTLV-III) From Patients With AIDS And Pre-AIDS" <i>Science</i> , 224:497-500.
A154	Saltarelli, M. J., et al. (1993) "The CAEV tat Gene Transactivates The Viral LTR And Is Necessary For Efficient Viral Replication" <i>Virology</i> , 197:35-44.
A155	Urdea, M. S., (1993) "Synthesis And Characterization of Branched DNA (bDNA) For The Direct And Quantitative Detection Of CMV, HBV, HCV, and HIV" <i>Clin. Chem.</i> 39:725-726.
A156	Allain, J., et al. (1987) "Long-Term Evaluation Of HIV Antigen And Antibodies To p24 And gp41 In Patients With Hemophilia" <i>N. Engl J. Med.</i> , 317:1114-1121.
A157	Barre-Sinoussi, F. et al. (1983) "Isolation Of A T-Lymphotropic Retrovirus From A Patient At Risk For Acquired Immune Deficiency Syndrome (AIDS)" <i>Science</i> 220:868-871.

	A158	Geodert, J. J., et al. (1987) "Effect Of T4 Count And Cofactors On The Incidence Of AIDS In Homosexual Men Infected With Human Immunodeficiency Virus", Jama 257:331-334.
	A159	Database Medline, US Nat. Lib., No. 97151131, Filocamo, G. et al. "Chimeric Sindbis Viruses dependent on NS3 protease of hepatitis C virus" J of Virology, (1997) 71(2):1117-27.

EXAMINER	JAN 14 2004	DATE CONSIDERED
----------	-------------	-----------------

\*EXAMINER: If reference considered, whether or not citation is in conformance with **MPEP 609**; Draw line through citation if not in conformance and not considered. **MADE** copy of this form with next communication to applicant.